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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/556,220	12/04/2006	Craig B. Thompson	UPN0012-100	4279
34136	7590	03/25/2010	EXAMINER	
Pepper Hamilton LLP 400 Berwyn Park 899 Cassatt Road Berwyn, PA 19312-1183			LOVE, TREVOR M	
			ART UNIT	PAPER NUMBER
			1611	
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			03/25/2010	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/556,220	<b>Applicant(s)</b> THOMPSON ET AL.	
	<b>Examiner</b> TREVOR M. LOVE	<b>Art Unit</b> 1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 03 August 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-10, 12-21, 23-26, 36, 49-52 and 58-67 is/are pending in the application.
- 4a) Of the above claim(s) 9 and 21 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-8, 10, 12-20, 23-26, 36, 49-52 and 58-67 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)         | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)         | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____   | 6) <input type="checkbox"/> Other: _____                          |

### **DETAILED ACTION**

Acknowledgement is made to Applicant's response filed 08/03/2009.

Claims 1-10, 12-21, 23-26, 36, 49-52, and 58-67 are pending.

Claims 9 and 21 are withdrawn.

Claims 1, 8, 10, 12, 16, 19, 20, 23-26, and 52 are currently amended.

Claims 58-67 are newly added.

Claims 1-8, 10, 12-20, 23-26, 36, 49-52, and 58-67 are currently under consideration.

Note: Applicant's election of record includes:

Invention I (claims 1-26, 35-37, and 49-53)

Glioblastoma cells as the cancer cell species

Hydroxycitrate as the ATP citrate lyase inhibitor species

Phosphoenolpyruvate as the tricarboxylate inhibitor species

Note: claim 16 is improperly identified as "previously presented", claim 16 should be identified as "currently amended".

### **Withdrawn Rejections**

The rejection of claims 8 and 20 under 35 U.S.C. 112, second paragraph, as being indefinite in that it fails to point out what is included or excluded by the claim language has been withdrawn in view of Applicant's amendments to said claims.

The rejection of claims 1, 4-8, 10-11, 14-15, 50-53 under 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837) is withdrawn in view of

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Applicant's cancellation of claims 11 and 53, and the New Grounds of Rejection set forth below.

The rejection of claims 16-20, 22, 25-26, 35-37, and 49 under 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837), in view of Bru et al. (US Patent 5,219,846) is withdrawn in view of Applicant's amendments to the claims, Applicant's cancellation of claims 22, 35, and 37, and the New Grounds of Rejection set forth below.

The rejection of claims 23-24 under 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837), in view of Bru et al. (US Patent 5,219,846), and further in view of Schroder et al. (Schroder et al. The role of 18F-fluoro-deoxyglucose positron emission tomography (18F-FDG PET) in diagnosis of ovarian cancer. Int. J. Gynecol Cancer. 1999;9:117-122) is withdrawn in view of Applicant's amendments to the claims and the New Grounds of Rejection set forth below.

### **Rejections and/or Objections**

- Maintained and Made Again - in view of amendments**
- New Grounds - in view of amendments and newly added claims**

### ***Claim Objections***

Claims 4-6 are objected to because of the following informalities: the claims recite "...effective amount of a an ATP...". Appropriate correction is required.

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***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

**Claims 1-8, 10, 12-15, 50-52, and 58-65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer). The**

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rejection of claims 2-3 and 12-13 is maintained and made again, and the rejection of claims 1, 4-8, 10, 14, 15, 50-52, and 58-65 is a new grounds of rejection.

Kuhajda teaches methods of treating carcinomas comprising administering a compound that inhibits fatty acid synthase (FAS), including inhibitors of citrate lyase such as hydroxycitrate (see Abstract, column 3, line 52-54 and column 11, lines 22-34 and 60). Kuhajda teaches that since many tumor cells are extremely dependent on endogenous fatty acid synthesis, lower FAS activity levels need not exclude a specific tumor as a candidate for therapy with fatty acid synthase inhibitors (see column 7, lines 61-64). Kuhajda teaches that it is advantageous to combine the active of Kuhajda with chemotherapeutic agents to target rapidly cycling cells (see column 8, lines 53-65). Kuhajda teaches that the presence of FAS in cells of the carcinoma may be detected by any suitable method, including activity assays, stains, and immunoassays (see column 7, line 65 to column 8, line 22).

Kuhajda fails to directly teach that the cancer is identified as comprising cancer cells that have a high rate of aerobic glycolysis, that said cancer is identified by PET imaging utilizing  $^{18}\text{F}$ -fluoro-deoxyglucose ( $^{18}\text{F}$ -FDG), or that said cancer is glioma.

Schroder teaches the role of  $^{18}\text{F}$ -fluoro-deoxyglucose positron emission tomography ( $^{18}\text{F}$ -FDG PET) in diagnosis of cancer. Schroder states that the clinical significance and usefulness of PET has been proven for a variety of malignant tumors, and specifically names glioma (see page 117, columns 1 and 2). Schroder teaches that “[i]n 1931 Warburg demonstrated that malignant tumors are characterized by an elevated aerobic and anaerobic glycolysis” (see page 117, first sentence).

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It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the  $^{18}\text{F}$ -FDG PET imaging as taught by Schroder to diagnose a patient with cancer for treatment with the composition of Kuhajda. One would have been motivated to do so since Schroder teaches that  $^{18}\text{F}$ -FDG PET imaging is useful in diagnosing malignant cancers, which, according to Warburg as cited by Schroder, necessarily comprises elevated aerobic glycolysis. There would be a reasonable expectation of success in utilizing the diagnostic method of Schroder to diagnose a carcinoma which is to be treated with the composition of Kuhajda since Kuhajda teaches that the carcinoma may be detected by any suitable method (see Kuhajda, column 7, line 65 to column 8, line 22).

With regard to claims 14, 15, 50, 51, 61, and 62 it would have been obvious to one of ordinary skill in the art at the time the invention was made to treat a cancer patient with a FAS inhibitor and a different chemotherapeutic agent or radiation therapy to control tumor growth. One would have been motivated to do so because Kudhajada suggest that FAS inhibitors may be utilized in conjunction with other therapeutic programs, wherein Kudhajada states that chemotherapy and radiation therapy are the most common forms of tumor treatment (see column 1, lines 36-43 and column 8, lines 58-65).

**Claims 1-8, 10, 12-20, 23-26, 36, 49-52, and 58-67 are rejected under 103(a) as being unpatentable Kuhajda et al. (US Patent 5,759,837, Patent issued Jun. 2, 1998), in view of Schroder et al. (1999, Int. J. Gynecol Cancer) as applied to claims**

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**1-8, 10, 12-15, 50-52, and 58-65, and further in view of Bru et al. (US Patent 5,219,846, Patent issued Jun. 15, 1993).** This is a New Grounds of Rejection.

The teachings of Kuhajda and Schroder are set forth above under the discussion of claims 1-8, 10, 12-15, 50-52, and 58-65.

Kuhajda and Schroder fail to directly teach that the composition further comprises a tricarboxylate transporter inhibitor, namely phosphoenolpyruvate (elected species).

Bru teaches methods for treating human tumors, particularly tumors that have become resistant to chemotherapy comprising administering an effective amount of phosphoenolpyruvic acid (see Abstract and column 1, lines 41-64).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the phosphoenolpyruvic acid of Bru with the citrate lyase inhibitor (e.g. hydroxycitrate) of Kuhajda for additive anti-tumor effects. One would have been motivated to do so since Kuhajda teaches that FAS inhibitors (e.g. ATP lyase inhibitors) can be combined with other chemotherapeutic agents and phosphoenolpyruvic acid as taught by Bru is a chemotherapeutic agent. It is further noted that MPEP 2144.05 states: ““It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art.” *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) (citations



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omitted). See also *In re Crockett*, 279 F.2d 274, 126 USPQ 186 (CCPA 1960); and *Ex parte Quadranti*, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992).

### *Response to Arguments*

It is noted that the majority of the rejections previously presented have been withdrawn. However, in view of the same references being relied upon, Applicant's arguments are still addressed.

Applicant argues in the remarks filed 08/03/2009 that Kuhajda fails to teach identifying the cancer as comprising cancer cells which have a high rate of glycolysis, and therefore, the reliance upon Kuhajda alone is improper. Applicant's arguments have been fully considered and are found persuasive. As such, the new grounds of rejection is based on Kuhajda in view of Schroder. Applicant's arguments do not overcome the rejection based on Kuhajda in view of Schroder since Schroder provides clear teaching that malignant tumors comprise elevated aerobic glycolysis. Applicant further argues that nothing in the references teaches or suggests that cancer characterized by a high rate of aerobic glycolysis is particularly susceptible to treatment involving the inhibition of citrate lysase. Applicant's argument is not found persuasive since first, it is noted that the art is not required to teach the same reasoning for adding components as Applicant, MPEP 2144 (IV) states "the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by Applicant. See,

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e.g., *In re Kahn*, 411 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006).” Second, motivation exists in *Kuhajda* to utilize known diagnostic techniques to identify the cancer, wherein *Schroder* clearly teaches that identification with  $^{18}\text{F}$ -FDG PET is well known in the art to identify cancers, particularly cancers with elevated aerobic glycolysis. Therefore, Applicant's arguments are not found persuasive. Furthermore, Applicant's arguments with regard to *Kuhajda* in view of *Bru* are moot in view of all of the rejections now including the *Schroder* reference which cures the deficiencies of *Kuhajda*.

### ***Conclusion***

No claims allowed. All claims rejected. No claims objected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to TREVOR M. LOVE whose telephone number is (571)270-5259. The examiner can normally be reached on Monday-Thursday 7:30-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached on 571-272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TL

/David J Blanchard/  
Primary Examiner, Art Unit 1643